REMARKS

Claims 1-7 and 18-19 are pending in this application. Applicant's Response to Final Office Action filed July 15, 2008 is incorporated herein by reference in its entirety. This paper is being filed on the presumption that Applicant's Response to Final Office Action filed July 15, 2008 has been entered into the record. In addition to the reasons set forth in Applicant's Response to Final Office Action filed July 15, 2008, Applicant respectfully submits that the pending claims are allowable for these additional reasons.

I. There are sufficient unexpected results to rebut even a *prima facie* case of obviousness.

On page 2 of the Office Action, the Examiner has maintained the rejection of claims 1-7, 18, and 19 under 35 U.S.C. §103(a) as being allegedly unpatentable over Muller *et al.*, U.S. Patent No. 6,020,358 in view of Tobinick, U.S. Patent No. 6,428,787, and D'Amato, U.S. Patent No. 6,235,756. In Applicant's Response to Final Office Action filed July 15, 2008, Applicant pointed out that the Examiner has not established a *prima facie* case of obviousness. This reason alone requires that the rejection under 35 U.S.C. §103(a) be withdrawn.

However, for avoidance of any doubt regarding the nonobviousness of the instant claims, Applicant submits herein evidence of unexpected results, which rebuts any alleged *prima facie* case of obviousness. As well settled, even if a *prima facie* case of obviousness is established, the Examiner is required to consider all rebuttal evidence submitted by an applicant. *See In re Sullivan*, 498 F.3d 1345 (Fed. Cir. 2007); *see also* MPEP §2145. This requirement remains unchanged following the decision in *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 167 L.Ed.2d 705, 75 USLW 4289, 82 U.S.P.Q.2d 1385 (2007), as the Federal Circuit has made clear in *In re Sullivan*. 498 F.3d at 1351. As the Court explained, "[w]hen a patent applicant puts forth rebuttal evidence, the Board must consider that evidence." (*Id.* at 1351). Such rebuttal evidence includes "evidence of unexpected results." *Id.*, citing *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1369 (Fed. Cir. 2007).

Attached hereto for the Examiner's consideration is a declaration from Peter H. Schafer, Ph.D. ("Declaration"), which describes experiments that were performed to evaluate the efficacy of cyclopropyl-N-{2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-3-oxoisoindoline-4-yl}carboxamide ("the instant compound") in the

treatment of macular degeneration. As the Examiner will see, the oral administration of the instant compound to mice unexpectedly resulted in remarkably higher inhibition of laser-induced choroidal neovascularization compared to the intravitreal injection of Lucentis, which is a FDA-approved drug for the treatment of wet age-related macular degeneration.[1] (*See, e.g.*, Declaration, paragraph 13 and Figure 1). Further, the oral administration of the instant compound to rats unexpectedly resulted in similar inhibition of laser-induced choroidal neovascularization compared to intravitreal injection of Lucentis.[2] (*See, e.g.*, Declaration, paragraph 14 and Figure 2). Thus, Applicant has provided sufficient unexpected results that rebut any alleged *prima facie* case of obviousness. As such, Applicant respectfully requests that the rejection under 35 U.S.C. §103(a) be withdrawn.

II. Conclusion

No fee is believed due for the submission of this paper. However, if any fees are due for the submission of this paper or to avoid abandonment of this application, please charge them to Deposit Account No. 50-3013.

Respectfully submitted,

Date: **August 5, 2008**

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[1] Administration of the instant compound at 5 mg/kg BID resulted in a 69% reduction in the neovascular area, and the administration at 15 mg/kg resulted in 73% reduction in the neovascular area ($P<0.002$). The inhibition resulting from the intravitreal injection of Lucentis was 36% ($P=0.0913$ under Dunnett's Method; $P=0.0423$ under Student's t-test).

[2] Administration of the instant compound at 10 mg/kg BID resulted in a 61% reduction in the neovascular area, and administration at 25 mg/kg BID resulted in 65% reduction ($P<0.0001$). The inhibition resulting from the intravitreal injection of Lucentis was 62% ($P<0.0001$).